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REPORT

of the

Commission on Neurotropic Virus Diseases of the Board for
the Investigation of Epidemic
Diseases

U. S. Army

CLASSIFICATION CHANGED
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Arthur R. Lord
ARTHUR R. LORD
Major, MSC
Security Officer, SGO

December 1, 1941 - May 15, 1942

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In the fall of 1941 it became evident that epidemic encephalitis (viz. equine encephalomyelitis of eastern and western types, and St. Louis encephalitis) would represent the most important group of neurotropic virus diseases with which this Commission would have to contend. During the summer of 1941 at least one sizeable epidemic of encephalitis (type undetermined) did occur among U. S. troops (at least 16 cases) with no deaths, but with a fair number of examples of encephalitic sequelae requiring discharge of the patients from the service. Similarly in an epidemic of western equine encephalomyelitis which occurred among Canadian troops in Manitoba in the summer of 1941, there were no deaths but there was an appreciable percentage of serious sequelae.* Western equine encephalomyelitis in young adults often does not lead to gross evidence of residual cerebral damage, but, as a result of post-encephalitic personality changes, men are often rendered unfit for service.

There appears to be little doubt then that the "summer encephalitides" should be included as a new and serious military disease.

The Commission's current activities have, therefore, been mainly concerned with this group of diseases, as follows:

I To improve methods for the clinical diagnosis of encephalitis in the Army.

II To increase knowledge about the control of these infections in man and to make such knowledge available to the Army with all possible speed.

III To lay plans (based on last year's experience) for the field study of epidemics of encephalitis which may arise in the Army during the summer of 1942.

I DIAGNOSIS

Through the kindness of Lt. Col. S. Bayne-Jones and Lt. Douglass W. Walker, M.C., a summary (for the first third of 1942) of the diagnostic status of neurotropic virus diseases in the army (as of May 11th, 1942) is available. This summary appears in the Appendix, Section 24. It indicates that blood samples for diagnosis are being sent in to the Virus Laboratory of the Army Medical School with much more regularity than was the case in 1941. This is in direct response to the S.G.O., Circular Letter, No. 107, (October 22, 1941).

To supplement information contained in this Circular Letter, a visit was made by the Director of the Commission during March and April, 1942, to a number of camps and hospitals in Texas, Arizona, and California. The importance of serological diagnosis was stressed with medical officers in charge of the infectious disease service in these areas. In order to expedite the available diagnostic laboratory service for camps in the west, medical officers in the 8th Corps area and the Pacific States were notified that the G.W. Hooper Foundation Laboratory, Medical Center, San Francisco, Cal., was also available for diagnostic work on suspected cases of encephalitis and that duplicate blood samples (viz: samples in addition to those sent to Washington, D.C.) could be sent there. Arrangements are in progress to establish this supplementary diagnostic service in the west, on a smooth working basis.

Technique of Neutralization Tests Recommended for Army Use. Dr. Olitsky and his associates, with Drs. Sabin, Webster and Casals have obtained agreement on a standard neutralization test for the equine and St. Louis types of encephalitis virus which they consider suitable for routine clinical diagnostic use. Details of this test have been reviewed with Lt. Col. H. Plotz and Dr. Karl Meyer. Arrangements have been made with the former that whenever cases of encephalitis of unknown type or types appear to be reaching epidemic proportions in any given military area, then efforts should be redoubled to reach a diagnosis. Under these circumstances duplicate or extra blood samples shall be provided by (or

* See Appendix Section 24.

ordered by the Virus Laboratory of the Army Medical School) to be sent to Dr. L. T. Webster of the Rockefeller Institute where neutralization and complement fixation tests are to be repeated on these samples.

Emergency Autopsy Service. Among the more valuable methods of establishing a diagnosis of encephalomyelitis (during an epidemic) and of increasing knowledge with regard to various types of encephalitis is the proper use of autopsy material. For this reason two members of the Commission, Dr. A. B. Sabin and Dr. J. Dawson have been assigned the task of performing autopsies (see previous report) in the eastern half of the country, and arrangements are in progress to make this service available to the west coast military hospitals through the staff of the Hooper Foundation of San Francisco. An outline of the technique to be followed in the performance of these autopsies appears in the Appendix, Section 3a.

To date this service has only been utilized once by the Army. An account of this study appears in Appendix, Section 3b.

Serum Therapy. Two recent studies, viz: (a) Zichis and Shaughnessy and (b) Traub (Zentr. Bakt. 1 Abt. Orig., 1941, 147, 81) indicate that the use of antiserum may be beneficial in the treatment of experimental equine encephalomyelitic virus infection. Dr. Olitsky is now repeating these observations as to whether immune serum can be used effectively in the experimental animal and whether it can possibly be recommended for use in man.

New Type of Encephalitis. Dr. Sabin has reported to us that studies which he has just completed (as yet unpublished) indicate that the lymphogranuloma venereum virus can be the cause of severe meningoencephalitis in man. This form of meningoencephalitis may be expected to occur among troops in certain regions at home and abroad, and it is particularly important to keep it in mind since there is reason to believe that sulfonamide therapy may be of value. ✓

II CONTROL OF EPIDEMIC ENCEPHALITIS IN THE ARMY

It appears that there are four or five areas where these diseases are most likely to appear in this country during 1942. They include: (i) Texas; (ii) the Salt River Valley of Arizona; (iii) the San Joaquin Valley of California; (iv) the Yakima Valley of the State of Washington; and (v) a large area embracing southwestern Minnesota, the Dakotas, Nebraska, and Colorado.

In these areas special attention should be paid this summer to the control of this group of diseases and preparations should begin now for the consideration of the control measures which might be adopted.

Mosquito Control. As it is now accepted as a reasonable probability, that equine encephalomyelitis and St. Louis encephalitis are mosquito borne diseases, the subject of mosquito control measures in potential and actual epidemic areas becomes a definite problem for the Army Medical Officer and the Public Health Officer in these diseases. This subject was reviewed by the Director with some of the civil and medical authorities in areas where encephalitis was epidemic last year and it was suggested that vigorous steps be taken early in the season to investigate this aspect of the situation within any of the above areas where the disease may appear during the coming summer months. The Commission is preparing to lend assistance to this type of investigation. In the State of California the question is under careful scrutiny and a report² of their preliminary work has already appeared.

Vaccination.* The success which has followed the vaccination of horses against eastern and western encephalomyelitis in this country indicates that under certain circumstances we may begin to regard the vaccination of man, as a reasonable proposal. In civil life about 200 humans (most of them laboratory workers) have been vaccinated during the last 3 years. The Lederle Company is now offering for sale a formalinized chick embryo vaccine in large quantities which has been tested in man by the Commission; and preliminary results show that it yields

*Theoretical aspects of the question of vaccination in animals and man is discussed at some length by Dr. Olitsky and his coworkers in the Appendix, Section 4.

serological evidences of immunizing capacity (See Appendix, Section 5). From a theoretical standpoint at least, this vaccine could be called upon for emergency use against western equine encephalomyelitis.

The Lederle vaccine will be administered, on a voluntary basis, to about 5,000 Canadian farmers (between the ages of 21 and 50) during the months of May and June, 1942; and results of this first mass vaccination program will be studied by the Commission.

It has been estimated that there may be at least ⁷ recognized varieties of epidemic encephalitis³ to which our troops may be exposed, and no doubt there are other varieties of summer (or seasonal) encephalitides which are yet to be recognized.

The known strains include:

1. Eastern equine encephalomyelitis
2. Western equine encephalomyelitis
3. St. Louis encephalitis
4. Japanese B encephalitis
5. West Nile Virus (Smithburn)⁵
6. Russian Virus⁶

→ Preliminary work on immune reactions with the first 4 viruses in this list indicates that little in the way of cross immunity may be expected; in other words, there is no indication as yet that a vaccine made from one type of virus will confer immunity to more than one type of encephalitis.

The vaccination potentialities of encephalitic virus are being studied on an experimental basis by members of the Commission as follows:

1 & 2 Equine encephalomyelitis (eastern and western) by P. K. Olitsky, Isabel M. Morgan and R. W. Schlesinger at the Rockefeller Institute for Medical Research; and by the Department of Pediatrics at the University of Pennsylvania, the Johnson Foundation of Philadelphia, and the laboratories of the Sharp and Dohme Company at Glenolden, Pa. All of these groups are concerned with the advantages

of allantoic fluid as vaccine and also with questions of dosage, time intervals, and methods of measuring the immunological response. An account of their preliminary work appears in the Appendix, Section 6.

3 & 4 St. Louis and Japanese B Virus are being tested by A. B. Sabin at the Children's Hospital Research Foundation of the University of Cincinnati. Dr. Sabin has already been able to report the development of formalinized St. Louis and Japanese B virus mouse brain vaccine, one dose of which can immunize mice within one week.

A preliminary report of Dr. Sabin's experiments appears in the Appendix, Section 7 and it is the present immediate concern of the Commission to decide whether to proceed with the production of these two vaccines on a scale large enough to insure a supply of 50,000 doses of each type, St. Louis and Japanese B to be available to the Army within the next few months.

5 & 6 West Nile Virus and Russian Virus are to be tested by L. T. Webster of the Rockefeller Institute.

Indications for Vaccination against Epidemic Encephalitis. It is too soon to state what the dangers of vaccinating humans against encephalitis may be, but information on this point should be available in the course of a few weeks (after the Canadian experiment). It is our opinion that all such encephalitic vaccine should be administered to soldiers during the summer of 1942 on a voluntary basis only.

The indications for vaccination are as follows:

1. If a sharp epidemic of western equine encephalomyelitis (confirmed by serological tests) should appear during the summer of 1942 in areas into which it will be necessary to send fresh (unexposed) troops during the epidemic season, we believe that such troops should be given the opportunity to choose if they would like to take the vaccine. Controls should automatically appear in an "experiment" of this type.

2. If western equine encephalomyelitis should break out in one area where troops are already quartered the judicious and voluntary use of the vaccine on certain bodies of troops (among which there should be a certain number of control groups) is indicated.

III EPIDEMIOLOGICAL STUDIES

The most important facts as to how the "seasonal encephalitides" are spread in this country probably remain to be settled. Consequently, vigorous work in the field should be conducted in various epidemic areas during the coming summer. Although the distribution of the equine encephalitides in the horse is widespread in this country, the endemic (and epidemic) distribution of these diseases (together perhaps with St. Louis encephalitis) in man is much more limited. The endemic distribution of the disease in man, covering a 5 year period has been recognized in the San Joaquin Valley in California,⁷ whereas epidemics of western equine and St. Louis have been reported in man within the past 2 years in the Salt River Valley of Arizona,⁸ the Yakima Valley of the State of Washington,⁹ and the upper Rio Grande Valley in New Mexico and Texas. Epidemics of western equine have appeared periodically (1937, 1938 and 1941) in Minnesota, the Dakotas and the adjoining southern states,¹⁰ as well as the northern provinces of Saskatchewan at Manitoba."

In an attempt to determine the host range, the most important animal or bird reservoirs, and the mosquito or other insect vectors, epidemiological surveys have been conducted in the civil populations by the Hooper Foundation, by the U.S. Public Health Service and the State Department of Health of Minnesota. All of these departments have been personally consulted and their advice has been solicited as to how to proceed on such studies for the Army.

It is agreed that an epidemiological field team for this type of work should consist of:

- 2 Entomologists (each with own assistant)
- 1 Zoologist (mammologist, ornithologist, or veterinarian)
- 1 Clinical Epidemiologist

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This team should work out of a central laboratory which must be prepared to test for living virus in mice and guinea pigs and to perform neutralization and complement fixation tests. New techniques have been suggested for these tests by Dr. Olitsky utilizing the chick embryo. See Appendix, Section 8. Members of the Commission and affiliates, are also prepared to go into the field this summer to perform studies of this kind.

In conclusion, I wish to express my appreciation for the hospitable and whole-hearted manner in which members of the Medical Corps of the U. S. Army have cooperated with us in the contacts which the Commission has had with the Army.

Yours respectfully,

John R. Paul, M.D.
Director, Commission on Neurotropic
Virus, Diseases, U. S. Army

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APPENDIX

Section 1

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(a)

Clinical Investigation of residual post-encephalitic effects in Canadian Army personnel. Through the courtesy of Colonel P. G. Bell, C. A. M. C., District Medical Officer, (M.D. #10) of Winnipeg, Canada, we had the privilege on April 24th and 25th, 1942 of reviewing the medical histories of 22 men in the Canadian Army who acquired encephalitis (in Manitoba) in August 1941. The diagnosis of equine encephalomyelitis of the western type was confirmed serologically (by complement fixation test at the Rockefeller Institute) in 6 of these cases.

Our review of these Canadian cases reveals the fact that, although there were no fatalities, bad sequelae (from the military standpoint) in the form of "post-encephalitic personality changes" occurred in a fair number of cases. The Canadian experience is as follows:

No. of cases investigated	22
No. of cases transferred and lost	10
No. followed for 6 months	12
No. discharged from the Canadian Army for post-encephalitic syndrome	5
No. discharged from the Canadian Army for other reasons, viz.	2
(a) Duodenal ulcer	
(b) Accidental gunshot wound	

(b)

Epidemic at Fort Sam Houston. This compares with the experiences at Fort Sam Houston where an epidemic of encephalitis (type undetermined) occurred in August 1941 (personal report of Lt. Colonel J. C. Woodland, M. C.). Of 16 cases diagnosed epidemic encephalitis several have shown "personality changes" during the subsequent 8 months.

Conclusions. The type (or types) of seasonal epidemic encephalitis now prevalent in the western half of this continent represent diseases with sequelae of sufficient seriousness to warrant the expenditure of time and effort in order to improve methods of diagnosis, therapy and prevention in this disease.

* Cases listed at Fort Osborne Barracks, Winnipeg, Manitoba, Canada.